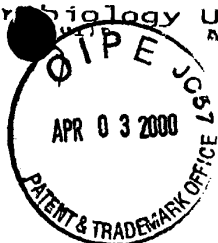


ALLIA.143A



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : H. Zaghouni

Appl. No. : 08/779,767

Filed : January 7, 1997

For : COMPOUNDS,
COMPOSITIONS AND
METHODS FOR THE
ENDOCYTIC
PRESENTATION OF
IMMUNOSUPPRESSIVE
FACTORS

Examiner : Patrick J. Nolan, Ph.D.

) Group Art Unit 1644

) I hereby certify that this correspondence and all
) marked attachments are being deposited with
) the United States Postal Service as first-class
) mail in an envelope addressed to: Assistant
) Commissioner for Patents, Washington, D.C.
) 20231, on

March 29, 2000

(Date)

Daniel Hart, Reg. No. 40,637

DECLARATION UNDER 35 U.S.C. §§1.132

1. This Declaration is being submitted to demonstrate that the compositions claimed in the above-identified application permanently eliminate the symptoms of autoimmune disease in all subjects treated.
2. I am an inventor on the above-identified application and am familiar with the specification and prosecution history.
3. I am skilled in the fields of immunology and molecular biology as evidenced by the accompanying curriculum vitae (Exhibit A).
4. The autoimmune disease experimental allergic encephalomyelitis (EAE), an animal model for multiple sclerosis, was induced in 6-8 week old mice by injecting them subcutaneously in the footpads with 100 µg of PLP1, a fragment of myelin proteolipid protein. The PLP1 peptide was administered in 200 µl incomplete Freund adjuvant IFA/PBS solution containing 200 µg *Mycobacterium tuberculosis* H37Ra and 100 µg of free PLP1 peptide. Six hours later, the mice were given 5×10^9 inactivated *Bordetella pertussis*. A second injection of *Bordetella pertussis* was given after 48 hours. Subsequently, the mice were scored daily for

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- clinical signs of EAE as follows: 0 no clinical score, 1 loss of tail tone, 2 hindlimb weakness, 3 hindlimb paralysis, 4 forelimb paralysis, and 5 moribund or death.
5. When signs of paralysis became apparent, the mice were treated with 500 µg of Ig-PLP-LR, an immunoglobulin containing the T cell receptor antagonist PLP-LR therein, on days 9, 13, and 17 post disease induction. Control mice received 500 µg of Ig-W, the parental immunoglobulin of Ig-PLP-LR which does not have a peptide inserted therein, on days 9, 13 and 17 post disease induction. The mice were then scored daily for clinical signs of EAE.
 6. Exhibit B illustrates the results of the above experiment. Each point represents the mean clinical score of 8 mice, with closed circles indicating the results obtained in mice receiving Ig-PLP-LR and open circles indicating the results obtained in the control mice. As depicted in Exhibit B, the mice treated with the control immunoglobulin developed EAE and did not recover for the 120 day period of observation. However, all of the mice treated with Ig-PLP-LR developed milder symptoms during the initial stages of treatment, fully recovered by 50 days post disease induction, and never relapsed.
 7. The results of this experiment indicate that treatment with immunoglobulins having a T cell receptor antagonist therein permanently eliminated disease symptoms in all of the animals tested.
 8. Without being limited to a particular mechanism of action, it is believed that replication of the pathogenic T cells induced by the PLP peptide was prevented by administration of the claimed compositions.
 9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: March 29, 2000

By: 
 Habib Zaghouani

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 031500

CURRICULUM VITAE

HABIB ZAGHOUBANI, PH.D.

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 Department of Microbiology
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Education

Ph.D.	1987	Immunology, University of Paris/Cancer Research Institute, Paris, France.
M.S.	1983	Immunology, University of Paris/Pasteur Institute, Paris, France.
B.S.	1981	Biochemistry, University of Paris, Paris, France.

Research experience

2000-present: Associate Professor, Microbiology, The University of Tennessee, Knoxville (recently promoted to Associate Professor, Official title pending approval by the President of the University)

1994-2000: Assistant Professor, Microbiology, The University of Tennessee, Knoxville.

1990-1994: Research Assistant Professor, Microbiology, Mount Sinai School of Medicine, New York.

1987-1989: Postdoctoral Fellow, Microbiology, Mount Sinai School of Medicine, New York. Advisor: Dr. Constantin A. Bona.

1983-1987: Graduate Research Assistant, Immunology, Cancer Research Institute, Paris, France. Mentor: Dr. Marc Stanislawski.

1981-1983: Graduate Research Assistant, Immunology, Pasteur Institute, Paris, France. Director: Dr. Arthur Dony Strosberg.

Teaching Experience

1992-1994: 600-level Immunology course, 3 credit hours, 6 lecture contact hours, 10 students, Spring Semester, Microbiology, Mount Sinai School of Medicine, New York.

1995-present: Microbiology 430 (Immunology), 3 credit hours, 45 lecture contact hours, 100-120 students, Fall Semester, Microbiology, The University of Tennessee, Knoxville.

1995-present: Co-direct Microbiology 602 (Microbial Pathogenesis Journal Club), 1 credit hour, 15 lecture contact hours, 10-15 students, Fall Semester, Microbiology, The University of Tennessee, Knoxville.

1995-present: Co-direct Microbiology 603 (Immunology Journal Club), 1 credit hours, 15 lecture contact hours, 10-15 students, Spring Semester, Microbiology, The University of Tennessee, Knoxville.

1995-Present: Microbiology 401 (Undergraduate Research), 3 credit hours, 1-2 students per semester, Microbiology, The University of Tennessee, Knoxville.

1998: Microbiology 630 (Topics in Immunology), 3 credit hours, 10 lecture contact hours, 20 students, Spring Semester, (Seminar Series) Microbiology, The University of Tennessee, Knoxville.

1998: Microbiology 493 (Independent Study in Immunology), 6 students, 10 lecture contact hours, Spring Semester, Microbiology, The University of Tennessee, Knoxville.

Honors and Awards

1999: Chancellor's nomination for Howard Hughes Medical Institute Assistant Investigator Appointment, The University of Tennessee, Knoxville (application pending).

1999: Biological Equipment Award, Office of Research Administration/Science Alliance/Genome Science and Technology/Division of Biology, The University of Tennessee, Knoxville.

1999: Science Alliance Research Excellence Award, Oak Ridge National Laboratories and The University of Tennessee, Knoxville.

1999: Exhibit, Performance, and Publication Expense Award, Faculty Senate Research Council and Office of research Administration, The University of Tennessee, Knoxville.

- 1998: Science Alliance Research Excellence Award, Oak Ridge National Laboratories and The University of Tennessee., Knoxville.
- 1998: Exhibit, Performance, and Publication Expense Award, Faculty Senate Research Council and Office of Research Administration, The University of Tennessee, Knoxville.
- 1997: Biological Equipment Award, Office of Research Administration/Science Alliance/ Division of Biology/ Department of Microbiology, The University of Tennessee, Knoxville.
- 1997: Exhibit, Performance, and Publication Expense Award, Faculty Senate Research Council and Office of Research Administration, The University of Tennessee, Knoxville.
- 1990: Research Excellence Award, Alliance Pharmaceutical Corporation. San Diego, CA.
- 1987-1988: Scientist Exchange Award (Postdoctoral Fellowship), French Cancer Society , Paris, France.
- 1984-1987: Graduate Student Scholarship, French Cancer Society, Paris, France.

Graduate Students and Postdoctoral Research Associates

1990-1992:	Honor Research Thesis	Daniel Goldstein, Mount Sinai School of Medicine, NY.
1995-present:	Ph.D. (expected 02/00)	Booki Min, The University of Tennessee, Knoxville.
1996-1998:	M.S.	Aimee Cestra, The University of Tennessee, Knoxville.
1996-present:	Ph.D (expected 09/00)	Kevin L. Legge, The University of Tennessee, Knoxville.
1997-present:	M.S. (expected 03/00)	Christopher Pack, The University of Tennessee, Knoxville.
1998-present:	Ph.D. (in progress)	Randal Gregg, The University of Tennessee, Knoxville.
1998-present:	M.D., Ph.D. (Postdoc)	Lequn Li, The University of Tennessee, Knoxville.
1999-present:	M.S. (in progress)	Jacque Caprio, The University of Tennessee., Knoxville.
2000-present:	Ph.D., (in progress)	Jeremiah Bell, The University of Tennessee, Knoxville.

Graduate Degree Committees

1995-1998:	M.S. Microbiology	Jack McPherson, The University of Tennessee, Knoxville.
1996-1998:	M.S. Microbiology	Aimee Cestra, The University of Tennessee, Knoxville.
1996-1999:	Ph.D. Microbiology	Sangjun Chun, The University of Tennessee, Knoxville.
1997-1999:	M.S. Microbiology	Kristin Lavander, The University of Tennessee, Knoxville.
1997-1999:	M.S. Microbiology	Amanda Royer, The University of Tennessee, Knoxville.
1996-present:	Ph.D. Microbiology	Booki Min, The University of Tennessee, Knoxville.
1997-present:	Ph.D. Microbiology	Kevin Legge, The University of Tennessee, Knoxville.
1998-present:	Ph.D. Microbiology	Shilpa Desphande, The University of Tennessee, Knoxville.
1999-present:	M.S. Microbiology	Christopher Pack, The University of Tennessee, Knoxville.

Professional Service

- 1992-present: Editorial board member: *Viral Immunology*
- 1992-present: Reviewer: *The Journal of Immunology*
- 1993-present: Reviewer: *Molecular Immunology*
- 1993-present: Reviewer: *Autoimmunity*
- 1995-present: Member of The Graduate Student Recruitment Committee, Department of Microbiology, The University of Tennessee, Knoxville.
- 1996-present: Reviewer: *Infection and Immunity*
- 1996-present: Reviewer: *Cellular Immunology*
- 1998: Member of Faculty Search Committee, Department of Comparative Medicine, College of Veterinary Medicine, The University of Tennessee, Knoxville.
- 1999: Panel Member: NIH/NCI, Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) Grant program. Flexible system to advance innovative research for cancer drug discovery by small business panel.

Professional Membership

1992-present: Member of the American Association for the Advancement of Science.
 1992-present: Member of the American Association of Immunologists.
 1998-present: Member of the Society for Neuroscience

Invited Speaker

2000 Division of Research, Alliance Pharmaceutical Corporation, San Diego, CA
 1999: Division of Research, Alliance Pharmaceutical Corporation, San Diego, CA.
 1999: Keystone Symposia, Immunogenetics of Human Disease, MHC/TCR & Peptide, Taos, NM.
 1999: Immunobiology Center, Mount Sinai School of Medicine, New York, NY.
 1999: Department of Microbiology, The University of Tennessee, Knoxville, TN.
 1998: Division of Research, Alliance Pharmaceutical Corporation, San Diego, CA.
 1997: Division of Research, Alliance Pharmaceutical Corporation, San Diego, CA.
 1997: Center for Neurologic Diseases, Harvard Medical School, Boston, MA.
 1997: Department of Microbiology, Vanderbilt School of Medicine, Nashville, TN.
 1996: Department of Microbiology, University of Tennessee, Knoxville, TN.
 1996: Division of Research, Alliance Pharmaceutical Corporation, San Diego, CA.
 1995: Department of Neurology, University of Alabama, Birmingham, AL.
 1995: Department of Biochemistry, Molecular & Cell Biology, The University of Tennessee, Knoxville, TN.
 1994: The Molecular and Immunological basis of Development of Vaccines, Fondation Merieux, Annecy, France.
 1993: Department of Microbiology, College of Biological Sciences, Columbus, OH.
 1993: Department of Microbiology, Dartmouth School of Medicine, Hannover, NH.
 1993: Unite d'Immunologie Cellulaire et Clinique, Institut Curie, Paris, France.
 1993: Research Division, Southwest Foundation for Biomedical Research, San Antonio, TX.
 1993: Department of Microbiology, Evansville Center for Medical Education, Evansville, IN.
 1990: International Conference on Cellular and Molecular Aspect of Self Reactivity and Autoimmune Diseases, Taormina, Italy.
 1992: Department of Microbiology, Medical College of Pennsylvania, Philadelphia, PA.
 1992: Federation of American Societies for Experimental Biology, Anaheim, CA.
 1991: Federation of American Societies for Experimental Biology, Atlanta, GA.
 1990: Centre de Recherche en Virologie, Institut Armand-Frappier, Laval, Quebec, Canada.

Research Grant Support

Active

- 1). RG2967A2/1, National Multiple Sclerosis Society, April 99 - March 2002. Down-regulation of encephalitogenic T cells. Direct cost: \$290,934/3years.
- 2). RO1101564, Astral Inc., March 95 - February 2001. A novel approach to delete encephalitogenic T cells. Direct cost: \$365,000/6 years.
- 3). 1RO1NS/AI37406, National Institutes of Health, January 2000- December 2002. Modulation of autoreactive T cells. Direct cost: \$491,415/3years.

Pending

- 1). National Institutes of Health, Regulation of Neonatal Immunity . Direct Cost: \$908,265/5 years.

Previous Support

- 1). RG2778A1/1, National Multiple Sclerosis, April 96 - March 1999. A deletional strategy for encephalitogenic T cells. Direct cost: \$ 252,573/3 years.
- 2). RO1101572, Astral Inc., September 97- August 99. Generation of human Ig chimeras carrying wild type or antagonist forms of myelin peptides. Direct cost:\$ 248,500/2 years

PUBLICATIONS

Manuscripts submitted for publication in peer-review Journals

40. Min, B., Legge, K. L., Li, L., Caprio, J. C., Gregg, R. K., Bell, J. J., and Zaghoulani, H. (2000). Defective up-regulation of IL-2 receptor alpha chain underlies interferon-gamma mediated T cell anergy. Submitted for publication.
39. Legge, K. L., Min, B., Caprio, J. C., Li, L., Gregg, R. K., Bell, J. J., and Zaghoulani, H. (2000). Coupling of peripheral tolerance to endogenous IL-10 promotes effective modulation of myelin-activated T cells and ameliorates experimental allergic encephalomyelitis. Being revised for J. Exp. Med.
38. Day, R. B., Okada, M., Ito, Y., Tsukada, K., Zaghoulani, H., Shibuya, N., and Stacey, G. (2000). Identification of a high affinity binding site of N-acetylchitooligosaccharides localized in the plasma membrane of soybean. Submitted for publication.

Manuscripts published in peer-review journals

37. Anderson, A. C., Nicholson, L. B., Legge, K. L., Turchin, V., Zaghoulani, H., and Kuchroo, V. K. (2000). High frequency of auto-reactive myelin proteolipid protein (PLP)-specific T cells in the periphery of naïve mice: mechanisms of selection of the self-reactive repertoire. J. Exp. Med. In press.
36. Min, B., Legge, K. L., Caprio, J. C., Li, L., Gregg, R., and Zaghoulani, H. (2000). Differential control of neonatal tolerance by antigen dose versus extended exposure and adjuvant. Cell. Immunol. In press.
35. Min, B., Legge, K. L., Li, L., Caprio, J. C., Pack, C. D., Gregg, R., McGavin, D., Slauson, D., and Zaghoulani, H. (1999). Neonatal tolerant immunity for vaccination against autoimmunity. Intl. Rev. Immunol. In press.
34. Legge, K. L., Min, B., Pack, C. D., Caprio, J. C., and Zaghoulani, H. (1999). Differential presentation of an altered peptide within fetal central and peripheral organs supports an avidity model for thymic T cell development and implies a peripheral re-adjustment for activation. J. Immunol. 162:5738-46.
33. Min, B., Legge, K. L., Pack, C. D. and Zaghoulani, H. (1998). Neonatal exposure to a self peptide-Ig chimera circumvents the use of adjuvant and confers resistance to autoimmune disease by a novel mechanism involving IL-4 lymph node deviation and INF γ -mediated splenic anergy. J. Exp. Med. 188:2007-17.
32. Legge, K. L., Min, B., Cestra, A.E., Pack, C. D., and Zaghoulani, H. (1998). T cell receptor agonist and antagonist exert in vivo cross-regulation when presented on immunoglobulins. J. Immunol. 161:106-11.
31. Legge, K. L., Min, B., Potter, N.T., and Zaghoulani, H. (1997). Presentation of a T cell receptor antagonist peptide by immunoglobulins ablates activation of T cells by a synthetic peptide or protein requiring endocytic processing. J. Exp. Med. 185:1043-53.
30. Brumeanu, T-D, Dehazya, P., Wolf, I., Bot, A., Bona, C., and Zaghoulani, H. (1996). Engineering of double antigenized Igs carrying B and T cell epitopes. Immunotechnology 2:85-95.

29. Brumeanu, T-D., Zaghouani, H., and Bona, C. (1995). Purification of antigenized immunoglobulins derivatized with monomethoxypolyethylene glycol. *J. Chromatogr.* 696:219-25.
28. Brumeanu, T-D., Zaghouani, H., Elahi, I., Daian, C. and Bona, C. (1995). Derivatization with monomethoxypolyethylene glycol of Igs expressing viral epitopes obviates adjuvant requirement. *J. Immunol.* 154:3088-95.
27. Zaghouani, H., Anderson, S., Sperber, K. E., Daian, C., Kennedy, R. C., Mayer, L. and Bona, C. (1995). Induction of antibodies to the human immunodeficiency virus type 1 by immunization of baboons with immunoglobulin molecules carrying the principal neutralizing determinant of the envelope protein. *Proc. Natl. Acad. Sci. USA.* 92:631-35.
26. Bona, C., Brumeanu, T-D and Zaghouani, H. (1994). Immunogenicity of microbial peptides grafted in self immunoglobulin molecules. *Cell. Mol. Biol.* 40 (suppl):21-30.
25. Brumeanu, T-D., Swiggard, W. J., Steinman, R. M., Bona, C., and Zaghouani, H. (1993). Efficient loading of identical peptide onto class II molecules by antigenized immunoglobulin and PR8 virus. *J. Exp. Med.* 178:1795-99.
24. Brumeanu, T-D., Kohanski, R., Bona, C., and Zaghouani, H. (1993). A sensitive method to detect defined peptide among those eluted from murine MHC class II molecules. *J. Immunol. Meth.* 160:65-71.
23. Kuzu, Y., Kuzu, H., Zaghouani, H., and Bona, C. (1993). Priming of CTLs at various stages of ontogeny with transfectoma cells expressing a chimeric Ig heavy chain gene bearing an influenza virus nucleoprotein. *International. Immunol.* 5:1301-07.
22. Zaghouani, H., Kuzu, Y., Kuzu, H., Swigard, W., Steinman, R., and Bona, C. (1993). Contrasting efficacy of presentation by major histocompatibility complex class I and class II products when peptides are administered within a common protein carrier, self immunoglobulin. *Eur. J. Immunol.* 23:2746-50.
21. Penney, C. L., Ethier, D., Dionne, G., Nixon-George, A., Zaghouani, H., Michon, F., Jennings, H., and Bona, C. (1993). Further studies on the adjuvanticity of stearyl Tyrosine and ester analogues. *Vaccine.* 11:1129-1134.
20. Kuzu, H., Kuzu, Y., Zaghouani, H., and Bona, C. (1993). In-vivo priming effect during various stages of ontogeny of an influenza virus nucleoprotein derived peptide. *Eur. J. Immunol.* 23:1397-1400.
19. Zaghouani, H., Steinman, R., Nonacs, R., Shah, H., Gerhard, W. and Bona, C. (1993). Efficient presentation of a viral T helper epitope expressed in the CDR3 region of a self immunoglobulin molecule. *Science.* 259:224-27.
18. Shengqiang, L., Polonis, V., Isobe, H., Zaghouani, H., Guinea, R., Moran, T., Bona, C., and Palese, P. (1993). Chimeric influenza virus induces neutralizing antibodies and cytotoxic T cells against human immunodeficiency virus type 1. *J. Virol.* 67:6659-66.
17. Zaghouani, H., Kuzu, Y., Kuzu, H., Mann, N., Daian, C., and Bona, C. (1993). Engineered immunoglobulin molecules as vehicles for T cell epitopes. *Int. Rev. Immunol.* 10:265-77.
16. Hall, B., Zaghouani, H., Daian, C. and Bona, C. (1992). A single amino acid mutation in CDR3 of the 3-14-9 light chain abolished expression of the IDA 10 defined idotype and antigen binding. *J. Immunol.* 149:1605-12
15. Nixon, A., Zaghouani, H., Penney, C. L., Lacroix, M., Dionne, G., Anderson, S., Kennedy, R. C. and Bona, C. A. (1992). Adjuvanticity of stearyl tyrosine on the antibody response to peptide 503-535 from HIV gp160. *Viral. Immunol.* 5:141-50

14. Zaghouani, H., Krystal, M., Kuzu, H., Moran, T., Shah, H., Kuzu, Y., Schulman, J. and Bona, C. (1992). Cells expressing a heavy chain immunoglobulin gene carrying a viral T cell epitope are lysed by specific cytolytic T cells. *J. Immunol.* 148:3604-09.
13. Zaghouani, H., Goldstein, D., Shah, H., Anderson, S., Lacroix, M., Dionne, G., Kennedy, R. C. and Bona, C. (1991). Induction of antibodies to the envelope protein of the human immunodeficiency virus by immunization with monoclonal anti-idiotypes. *Proc. Natl. Acad. Sci. USA.* 88:5645-49.
12. Kaushik, A., Mayer, R., Fidanza, V., Zaghouani, H., Lim, A., Bona, C. and Dighiero, G. (1990). LY-1 and V-gene expression among hybridomas secreting natural autoantibody. *J. Autoimmunity* 3:687-700.
11. Mayer, R., Zaghouani, H., Usuba, O. and Bona, C. (1990). The LY-1 gene expression in murine hybridomas producing autoantibodies. *Autoimmunity* 6:293-305.
10. Bonilla, F. A., Zaghouani, H., Rubin, M. and Bona, C. (1990). VK gene usage, idiotype expression, and antigen binding among clones expressing the VHx24 gene family derived from naive and anti-id immune Balb/c mice. *J. Immunol.* 146:616-22.
9. Fidanza, V., Mayer, R., Zaghouani, H., Diliberti, M. A., and Bona, C. (1990). Autoantibodies, LY-1 and immunoglobulin V gene expression in hybridomas obtained from young and old NZB mice. *Arthritis & Rheumatism.* 33:711-23.
8. Zaghouani, H., Bonilla, F. A., Meek, K. & Bona, C. (1989). Molecular basis for expression of the A48 regulatory idiotype on antibodies encoded by immunoglobulin variable region genes from various families. *Proc. Natl. Acad. Sci. USA.* 86:2341-45.
7. Zaghouani, H., Fidanza, V. and Bona, C. (1989). The significance of idiotype-anti-idiotype interactions in the activation of self reactive clones. *Clin. Exp. Rheumatology.* 7/S-3:S19-25.
6. Pinter, A., Honnen, W. J., Tilley, S. A., Bona, C., Zaghouani, H., Zolla-Pazner, S. and Gorny, M. (1989). Oligomeric structure of gp41, the transmembrane protein of human immunodeficiency virus type 1. *J. Virol.* 63:2674-79.
5. Zaghouani, H., Pene, J., Rousseau, V. and Stanislawski, M. (1988). A new strain specific cross-reactive idiotype with possible regulatory function expressed on Balb/c anti- $\alpha(1-3)$ dextran antibodies. *J. Immunol.* 140:3844-50.
4. Zaghouani, H., and Stanislawski, M. (1987). Regulation of the response to $\alpha(1-3)$ dextran: An anti-dextran associated idiotope of Balb/c mice is also expressed on A/J anti-NIP antibodies. *Mol. Immunol.* 24:1237-42.
3. Bara, J., Gautier, R., Zaghouani, H. and Decans, C. (1986). Monoclonal antibodies against oncofetal mucin M1 antigens associated with precancerous colonic mucosae. *Cancer Res.* 46:3983-89.
2. Pene, J., Rousseau, V., Zaghouani, H., Paroutaud, P., Strosberg, D. and Stanislawski, M. (1986). Monoclonal anti- $\alpha(1-3)$ dextran antibodies of Igha Balb/c and Igh^b C.B20 mice display striking similarities. *J. Immunol.* 137:2319-24.
1. Pene, J., Bekkoucha, F., Desaymard, C., Zaghouani, H., and Stanislawski, M. (1983). Induction of a cross-reactive idiotype dextran-positive antibody response in two IghC^b mouse strains treated with anti-J558 cross-reactive idiotype antibodies. *J. Exp. Med.* 157:1573-93.

Book Chapters and Reviews

7. Zaghouani, H., and Bona, C. (1992). Stimulation of lymphocytes by anti-idiotypes bearing the internal image of viral antigens. In *T Lymphocytes Structure, Function, Choices* (eds, Celada, F., and Pernis, B). NATO ASI SERIES, Series A: Lif Scienc s 233: 121-23.
6. Zaghouani, H., Hall, B., Shah, H. and Bona, C. (1991). Immunogenicity of synthetic peptides corresponding to various epitopes of the human immunodeficiency virus envelope protein. In *Adv. Exp. Med. Biol.* (ed, Atassi, Z). Plenum Press, New York. 303: 53-62
5. Mayer, R., and Zaghouani, H. (1991). Molecular studies on the contribution of the LY-1 B cell subset to self-reactivity. In *Molecular Immunobiology of Self Reactivity*. Immunology series. (eds, Bona, C. & Kaushik, A.) Marcel Dekker Publisher, New York. . 55: 61-79
4. Bonilla, F. A., Zaghouani, H. and Bona, C. (1990) Patterns of idiotypic similarity and their structural bases among antibodies specific for foreign and self antigens. In *Idiotype in Biology and Medicine*. (eds, Carson, D. A., Chen, P. P. and Kipps, T. J.). Prog. Chem. Immunol. Basel, Karger. 48:49-62.
3. Mayer, R., Zaghouani, H., Kaushik, A., Kasturi, K., Fidanza, V. and Bona, C. (1990). The expression of LY-1 and immunoglobulin variable gene families in hybridomas producing autoantibodies of various specificities. In *The Molecular Aspects of Autoimmunity*. (eds, Farid, N. R. and Bona, C.A.). Academic Press, PP 1-27.
2. Zaghouani, H., Victor-Kobrin, C., Barak, Z., Bonilla, F.A. and Bona, C. (1988). Molecular profile of monoclonal antibodies expressing the A48 regulatory idiotype and having distinct antigenic specificities. *Ann. New York. Acad. Sci.* 546:248-50.
1. Pene, J., Zaghouani, H., and Stanislawski, M. (1984). Regulation of the response to $\alpha(1-3)$ dextran in IgH^C mice. *Ann. New York. Acad. Sci.* 814:296-304.

Published Abstracts

About 12 abstracts were published in the last 5 years

Patents

- | | |
|------|--|
| 1992 | Anti-human immunodeficiency virus recombinant antibodies. Constantin Bona and Habib Zaghouani. Ussued in Australia (#18919 672580), Canada (#2107329), and Israel (101602), (April 1992), pending in Europe (#92911196.1) and Japan (#4[1992]510879) . |
| 1994 | Patent # 5,969, 109, chimeric antibodies comprising antigen binding sites and B and T cell epitopes, Constantin Bona and Habib Zaghouan. Issued October 19, 1999.. |
| 1997 | Compound, compositions and methods for the endocytic presentation of immunosuppressive factors. Habib Zagouani. Pending (#08/779,767) |

EXHIBIT B

